IN THE CLAIMS

Please replace prior versions and listings of claims in the application with the following set of claims.

Claims 1-37 are currently pending. Claims 38-44 were previously withdrawn in response to a restriction requirement.

Claims 1-37 are hereby amended. Claims 45 to 50 are added as noted below.

1. (Currently Amended) The method of synthesizing an oligonucleotide product for preferentially killing cancerous cells over non- cancerous cells comprising the steps of:

(a) Using a first oligonucleotide comprising a nucleotide sequence, N, and with at least two CpG moieties; and

(b) Covalently linking one or more units of an antimetabolite ((a)) prodrug ~~for an antimetabolite covalently linked to the~~ to said first oligonucleotide.

2. (Currently Amended) The ~~oligonucleotide~~ method of claim 1, wherein ~~the~~ said antimetabolite is selected from the group consisting of 2'-deoxy-3'-thiacytidine, 3'-azido-3'-deoxythymidine, 2',3'-dideoxycytidine, 2' ,3 '-didehydro-3'-deoxythymidine, 2',3'-dideoxyinosine, 5-fluoro-2' -deoxy uridine, 2-fluoro-9-b-D-arabinofuranosyladenine, I-B-Darabinofuranosylcytosine, 5-azacytidine, 5-aza-2'-deoxycytidine, 6-mercaptopurineriboside, 2-chlorodeoxyadenosine, and pentostatin.

3. (Currently Amended) The method ~~oligonucleotide~~ of claim 1, wherein ~~the~~ said ~~prodrug is a prodrug for the~~ anitmetabolite is 2'- deoxy, 2', 2'- difluorocytidine.

4. (Currently Amended) The method ~~oligonucleotide~~ of claim 1, wherein two of ~~the~~ said at least two CpG moieties are separated by a number of nucleotides, said number being selected from the group ~~numbers~~ 2, 5, and 9.

[illegible] of claim 1, wherein one of said one or more units of an antimetabolite prodrug is linked 5' to ~~the~~ one of said at least two CpG moieties.

6. (Currently Amended) The method ~~oligonucleotide~~ of claim 1, wherein one of said one or more units of an antimetabolite prodrug is linked 3' to ~~the~~ one of said at least two CpG moieties.

7. (Currently Amended) The method ~~oligonucleotide~~ of claim 1, wherein one of said one or more units of an antimetabolite prodrug is linked 3' to ~~the~~ one of said at least two CpG moieties and one of said one or more units of an antimetabolite prodrug is linked 5' to ~~the~~ one of said at least ~~a second~~ two CpG moieties.

8. (Currently Amended) The method ~~oligonucleotide~~ of claim 1, wherein said one or more units of an antimetabolite prodrug ~~is~~ are linked to ~~the~~ said first oligonucleotide by a 3'-3' linkage.

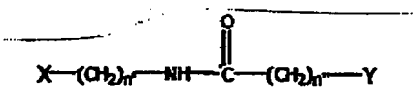
9. (Currently Amended) The method ~~oligonucleotide~~ of claim 1, wherein said one or more units of an antimetabolite prodrug ~~is~~ are linked to ~~the~~ said first oligonucleotide by a 5'-5' linkage.

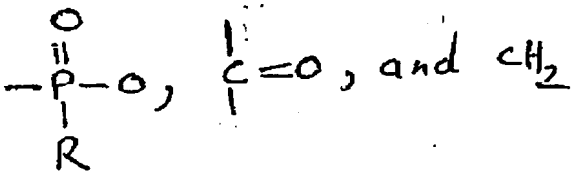
10. (Currently Amended) The method ~~oligonucleotide~~ of claim 1, wherein said one or more units of an antimetabolite prodrug ~~is~~ are linked to ~~the~~ said first oligonucleotide by a 3'-5' linkage.

11. (Currently Amended) The method ~~oligonucleotide~~ of claim 1, wherein said one or more units of an antimetabolite prodrug ~~is~~ are ~~covalently~~ linked to ~~the~~ said first oligonucleotide by a 5'-3' linkage.

12. (Currently Amended) The method ~~oligonucleotide~~ of claim 1, wherein one of said one or more units of an antimetabolite prodrug ~~is covalently~~ linked at a ~~position that is selected from 10 upstream s units from one of the said at least two CpO~~ moieties, s being a whole number between 2 and 50.

13. (Currently Amended) The method ~~oligonucleotide~~ of claim 1, wherein ~~the~~ one of said one or more units of an antimetabolite prodrug is ~~covalently~~ linked to ~~the~~ said first oligonucleotide by a linker having the formula.



wherein x and y are independently selected from 

and R is selected from OH, S, a C_1-C_6 alkyl, a C_1-C_6 alkoxy, and NH.

consisting of a phosphodiester linkage, a Cl-C6 alkoxy phosphotriester linkage, a phosphorothioate linkage and a phosphoramidate linkage.

21. (Currently Amended) A pharmaceutical composition ~~comprising a therapeutically effective amount of the oligonucleotide~~ made by a method of any of claims 1-20.

22. (Currently Amended) The ~~oligonucleotide~~ product of claim 21 wherein said ~~pharmaceutically acceptable carrier is~~ pharmaceutical composition comprises lipofectin as a carrier.

23. (Currently Amended) ~~An~~ The method of synthesizing an oligonucleotide product for preferentially killing cancerous cells over noncancerous cells comprising a ~~motif represented by the formula: 5'PGXCG3' wherein P is a prodrug for an antimetabolite and X represents between 0 and 50 nucleotides.~~ the steps of:

(a) Using a first oligonucleotide with at least one CpG moiety and comprising a nucleotide sequence, X, having between ((0)) 2 and 50 nucleotides; and

(b) Covalently linking a prodrug, P, for the antimetabolite 2'-deoxy, 2'-,2'-difluorocytidine to said first oligonucleotide so as to form PG, a second moiety of said oligonucleotide product.

24. (Canceled)

25. (Currently Amended) ~~An~~ The ~~oligonucleotide of claim 23~~ method of synthesizing an oligonucleotide product for preferentially killing cancerous cells over noncancerous cells comprising the steps of:

(a) Using a first oligonucleotide with at least one CpG moiety and comprising a nucleotide sequence, X, having between ((0)) 2 and 50 nucleotides; and

(b) Covalently linking a prodrug, P, to said first oligonucleotide, wherein ~~the metabolite~~ P is selected from the group consisting of 2'-deoxy-3'-thiacytidine, 3'-azido-3'-deoxythymidine, 2',3'dideoxycytidine,2',3'-didehydro-3'-deoxythymidine, 2',3'-dideoxyinosine, 5-fluoro-2'-deoxy uridine, 2-fluoro-9-b-D-arabinofuranosyladenine, 1-B-D-arabinofuranosylcytosine, 5 azacytidine, 5 aza-2'-deoxycytidine, 6-mercaptopurineriboside, 2 chlorodeoxyadenosine, and pentostatin.

26. (Currently Amended) The ~~method oligonucleotide~~ of claim of 23, where X is selected from the group consisting of 2, 5, and 9.

27. (Currently Amended) The ~~method oligonucleotide~~ of claim 23, wherein ~~the oligonucleotide comprises multiple nucleotides and the prodrug is covalently linked to one of the nucleotides by~~ said covalent link of P is a 3'-3' linkage.

28. (Currently Amended) The ~~method oligonucleotide~~ of claim 23, wherein ~~the oligonucleotide comprises multiple nucleotides and the prodrug is covalently linked to one of the nucleotides by~~ said covalent link of P is a 5'-5' linkage.

29. (Currently Amended) The ~~method oligonucleotide~~ of claim 23, wherein ~~the oligonucleotide comprises multiple nucleotides and the prodrug is covalently linked~~ to one of the nucleotides by said covalent link of P is a 3' 5' linkage.

30. (Currently Amended) The method ~~oligonucleotide~~ of claim 23, wherein ~~the oligonucleotide comprises multiple nucleotides and the prodrug is covalently linked to one of the nucleotides by~~ said covalent link of P is a 5'-3' linkage.

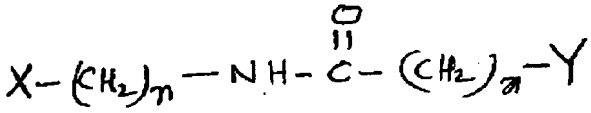
31. (Currently Amended) The method ~~oligonucleotide~~ of claim 23, wherein ~~the oligonucleotide comprises~~ X contains at least one nucleotide having a ribose sugar moiety.

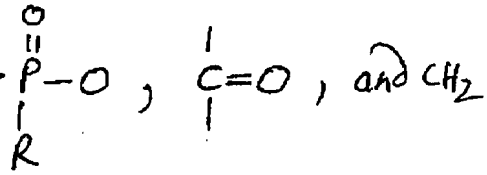
32. (Currently Amended) The method ~~oligonucleotide~~ of claim 23, wherein ~~the oligonucleotide comprises~~ X contains at least one nucleotide having a 2'-deoxyribose sugar moiety.

33. (Currently Amended) The method ~~oligonucleotide~~ of claim 23, wherein ~~the oligonucleotide~~ X comprises at least one nucleotide from the group ~~2'-O-alkyl~~ 2'-o-alkyl ~~nucleotide, one 2'-N-Alkyl~~ 2'-n-alkyl ~~nucleotide, or one~~ and ~~2'-O-halogen~~ 2'-o-halogen and nucleotide, wherein the alkyl has approximately having between about 1 and ~~about~~ 6 carbon atoms.

34. (Currently Amended) The method ~~oligonucleotide~~ of claim 23, wherein ~~the oligonucleotide~~ X comprises a plurality of nucleotides connected by covalent internucleoside linkages, wherein each of the linkages ~~are~~ is selected from the group consisting of a phosphodiester linkage, a C1-C6 alkoxy phosphotriester linkage, a phosphorothioate linkage and a phosphoramidate linkage.

35. (Currently Amended) The method ~~oligonucleotide~~ of claim 23, wherein ~~the oligonucleotide comprises multiple nucleotides and the prodrug~~ P is attached to at least one of the ~~multiple~~ nucleotides in X by a linker having the formula.



wherein x and y are independently selected from 

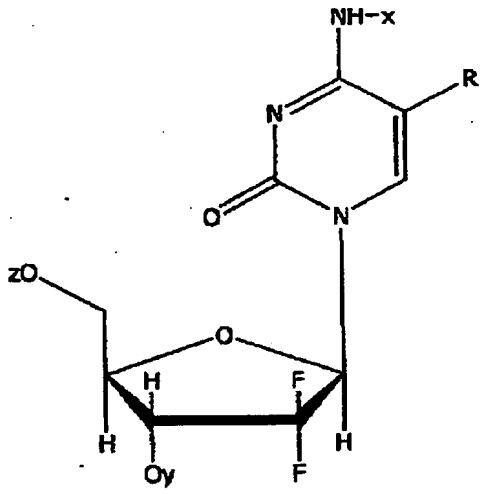
and R is selected from OH, S, a C_1-C_6 alkyl, a C_1-C_6 alkoxy, and NH.

36. (Currently Amended) A pharmaceutical composition ~~comprising a therapeutically effective amount of the oligonucleotide~~ made by the method of any of claims 23-35.

37. (Currently Amended) The ~~oligonucleotide~~ product of claim 36 wherein said ~~pharmaceutically acceptable carrier is~~ pharmaceutical composition comprises lipofectin as a carrier.

Claims 38 to 44 below are all Withdrawn

38. A compound having purity in excess of 98% by HPLC, having the formula:



wherein R is selected from the group consisting of H, a C1-C6 alkyl, a halogen, a C2-C6 alkenyl, and a C2-C6 alkynyl;

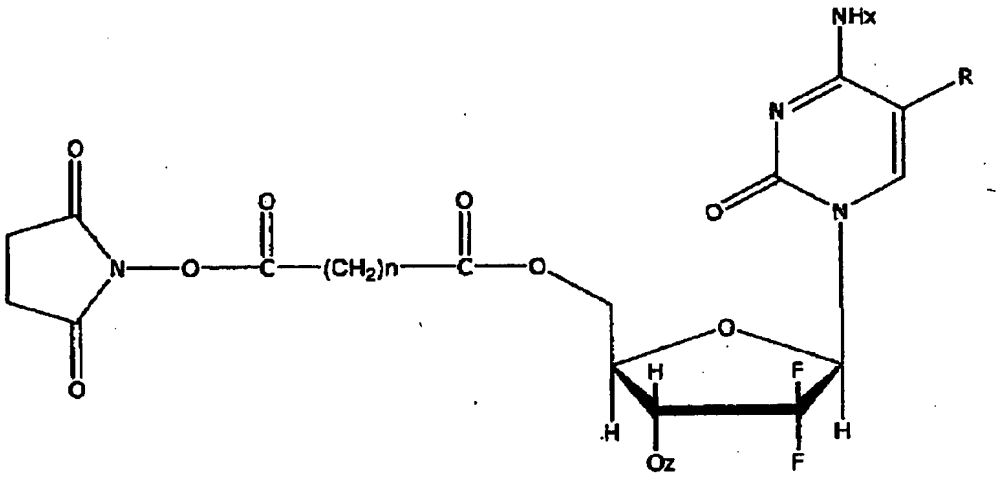
x is an amine-protecting group that is stable in oligonucleotide synthesis conditions; and

y, and z are each selected from H, a hydroxyl-protecting group that is stable in oligonucleotide synthesis conditions and a group that can be attached to a solid support.

39. The compound of claim 23, wherein the group that is attachable to a solid support has the formula O-C(=O)-M-C(=O)-NH-Spacer, where M is selected from the group consisting of succinyl, oxalyl, and hydroquinolynyl, and wherein the Spacer is selected from the

40. group consisting of a C1-C6 alkyl, ethyloxyglycol, and a combination of alkyl and ethyleneglycoxy.

41. A compound having the formula:



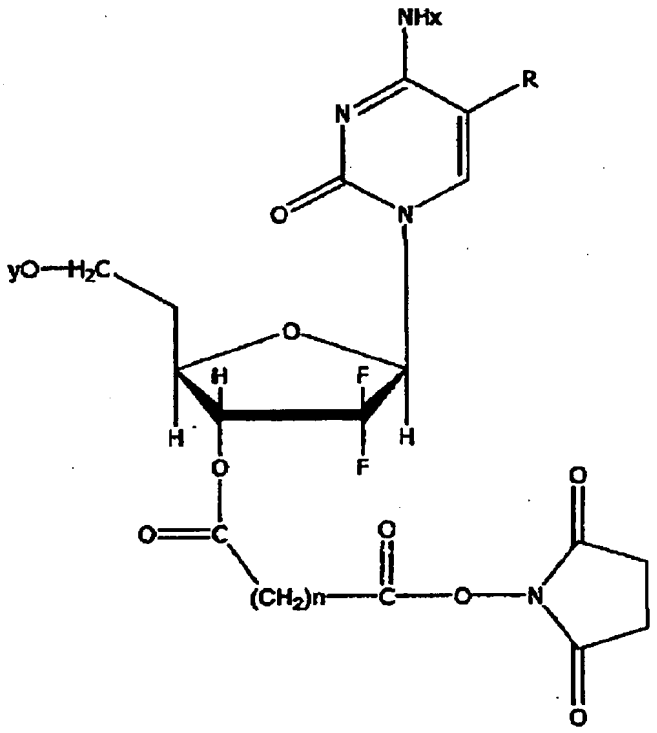
wherein R is selected from the group consisting of H, a C1-C6 alkyl, a halogen, a C2-C6 alkenyl, and a C2-C6 alkynyl;

x is an amine-protecting group that is stable in oligonucleotide synthesis conditions;

z is a hydroxyl-protecting group that is stable in oligonucleotide synthesis conditions; and

n is 2-20.

42. A compound of the formula:



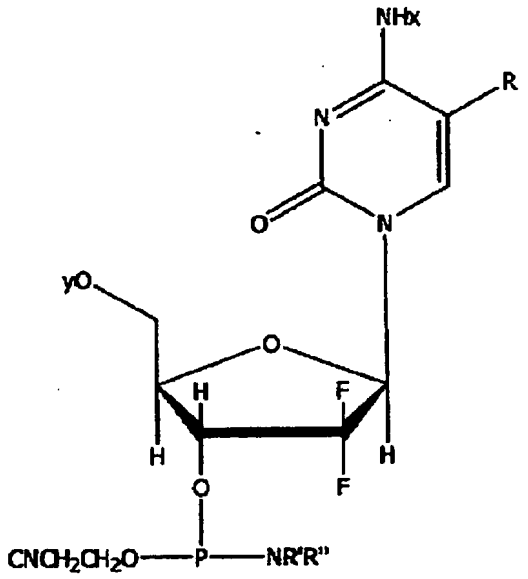
wherein R is selected from the group consisting of H, a C1-C6 alkyl, a halogen, a C2-C6 alkenyl, and a C2-C6 alkynyl;

x is an amine-protecting group that is stable in oligonucleotide synthesis conditions;

z is a hydroxyl-protecting group that is stable in oligonucleotide synthesis conditions; and

n is 2-20.

43. A compound having a purity in excess of 97% by HPLC, as shown by the formula:

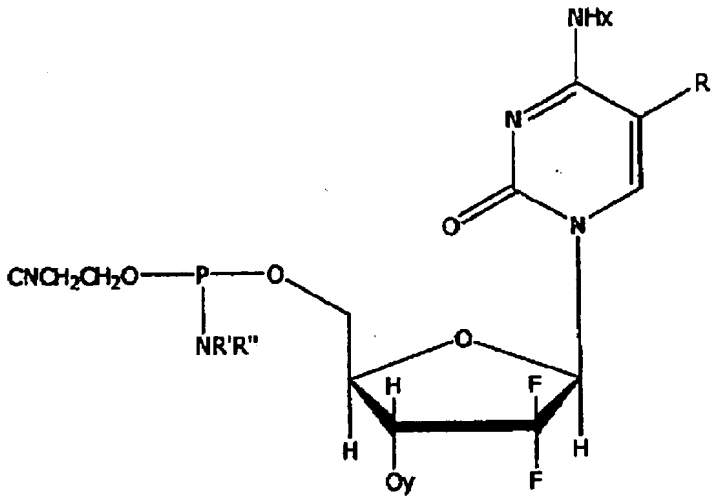


wherein y is a hydroxyl-protecting group that is stable in oligonucleotide synthesis conditions;

x is selected from the group consisting of H, a C1-C6 alkyl, a halogen, a C2-C6 alkenyl, and a C2-C6 alkynyl; and

R' and R'' are independently selected from the group consisting of a C1-C6 alkyl and a C2-C6 cycloalkyl.

44. A compound having purity in excess of 97 % by HPLC, and having the formula:



wherein y is a hydroxyl-protecting group that is stable in oligonucleotide synthesis conditions;

x is an amine-protecting group that is stable in oligonucleotide synthesis conditions,

R is selected from the group consisting of H, a C1-C6 alkyl, a halogen, a C2-C6 alkenyl, and a C2-C6 alkynyl; and

R' and R" are independently selected from the group consisting of a C1-C6 alkyl and a C2-C6 cycloalkyl.

(Claims 45-[illegible] are newly added)

45. (New) The method of claim 1, for preferentially killing cancerous cells in the colon, wherein said prodrug is antimetabolite dFC – 2'- deoxy, 2', 2'- [illegible], dFCG represents the first CpG moiety of said first oligonucleotide, and N is GGACG.

46. (New) The method of claim 1, for preferentially killing cancerous cells in the colon, wherein said prodrug is antimetabolite dFC = 2'- deoxy, 2', 2'- difluorocytidine, dFCG represents the first CpG moiety of said first oligonucleotide, and N is GTGGAA.

47. (New) The method of claim 1, for preferentially killing cancerous cells in the colon, wherein said prodrug is antimetabolite dFC = 2'- deoxy, 2', 2'- difluorocytidine, dFCG represents the first CpG moiety of said first oligonucleotide, and N is GGACGTGGAA.

48. (New) The method of claim 1, for preferentially killing cancerous cells in the colon, wherein said prodrug is antimetabolite dFC – 2'- deoxy, 2', 2'- difluorocytidine, dFCG represents the first CpG moiety of said first oligonucleotide, and N is G GAGCTGGAACG.

49 (New) A pharmaceutical composition of claim 21 comprising a therapeutically effective amount of said oligonucleotide product.

50. (New) A pharmaceutical composition of claim 36 comprising a therapeutically effective amount of said oligonucleotide product